

**REMARKS****I. Status of the Claims and Formal Matters**

Claims 1-7 and 9-26 are presently pending in this application. Claims 21 and 22 are withdrawn from consideration. Claims 1, 12, 17 and 26 are amended and new claims 27 and 28 have been added. No new matter has been added by the amendments or new claims. Support is found throughout the specification and from the pending and original claims.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the changes place the application in condition for allowance.

**II. The Rejections Under 35 U.S.C. § 112 Are Overcome**

Claim 26 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It is alleged that the limitation wherein “the second tissue is derived from amniotic membrane” is not described in the specification. Applicants respectfully traverse this rejection.

Claim 26, as amended recites the limitation “further comprising administration of amniotic membrane therapy.” This recitation is described at paragraphs 25 and 36 of the specification. See, paragraphs 25 and 36 of US Patent Application Publication No. 2002/0022606, published on February 21, 2002. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 is respectfully requested.

### **III. The Rejections Under 35 U.S.C. § 102(b) Are Overcome**

Claims 1-7, 9-14, 17-20 and 23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Khadem et al. Applicants respectfully traverse this rejection.

#### **A. Khadem Lacks Elements of the Claimed Invention**

To form the basis of a proper rejection under 35 U.S.C. § 102(b), a cited reference must disclose each and every element of the rejected claim(s). *See Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Khadem fails to disclose each and every element of the claimed invention and therefore, should be removed from consideration as a reference under 35 U.S.C. § 102(b).

Claim 1 is directed to a photochemical method of creating a tissue seal in the absence of an exogenous cross-linkable substrate. Claim 1 has been amended to further characterize the claimed tissue seal as having the tensile strength of the native tissue. Support for this amendment can be found at paragraph 49 of the specification. *See*, paragraph 49 of US Patent Application Publication No. 2002/0022606, published on February 21, 2002. Tensile strength is known in the art as the resistance of a material (e.g., a tissue) to a force that tears it apart, measured as the maximum tension the material can withstand without tearing.<sup>1</sup> A tissue seal created by the methods of amended claim 1 has a tensile strength of the native tissue, and therefore, is distinguished from the weaker “adhesive connection” allegedly described by Khadem (column 7 lines 18-30).

The Declaration of Dr. Khadem, submitted with Applicants responses dated November 17, 2004 (re-submitted on January 24, 2005 due to PTO error) and June 15, 2005, characterizes the strength of the “adhesive connection” allegedly described by Khadem (column 7 lines 18-30), wherein the photosensitizer composition applied to the tissue to form the connection contains less than 1% exogenous protein (i.e., this would include compositions having no exogenous protein). It was demonstrated by Dr. Khadem that use of less than 1% exogenous protein provides an adhesive connection in corneal tissue having a bursting pressure of 0.0 mm Hg, which is far below the intraocular pressure limit for a normal cornea. *See* paragraph 9 of the Khadem declaration. Therefore, the methods of Khadem that involve the use of a photosensitizer composition

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<sup>1</sup> A text book definition of “tensile strength” is submitted under Tab 1 for the Examiner’s reference.

containing less than 1% exogenous protein (e.g., including no exogenous protein) do not produce a tissue seal having the tensile strength of the tissue.

Claims 12 and 17 are directed to photochemical methods of repairing a corneal tissue without the use of an exogenous cross-linkable substrate. Claims 12 and 17 have been similarly amended, to specify that the intraocular pressure limit of the repaired corneal lesion is greater than 100 mm Hg. Support for this amendment can be found at paragraph 82 of the specification. See, paragraph 82 of US Patent Application Publication No. 2002/0022606, published on February 21, 2002. A corneal repair made by the methods of amended claims 12 and 17 has an intraocular pressure limit which is greater than 100 mm Hg, and is therefore distinguished from the corneal repair of Khadem using less than 1% exogenous protein and than having a bursting pressure of 0.0 mm Hg.

**B. Khadem is Not Enabled**

For a reference to be eligible under 35 U.S.C § 102(b), it must also be enabled. A reference is considered to be enabled only if “one of ordinary skill in the art could have combined the publication’s description of the invention with his [or her] own knowledge to make the claimed invention.” *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). See also, M.P.E.P. 2121.01. Applicants maintain and incorporate by reference the March 23, 2004 and June 13, 2005 Declarations of Dr. Michael Hamblin and the April 12, 2004, November 17, 2004 and June 15, 2005 Office Action responses (collectively referred to herein as “the Applicants’ submissions”) asserting that Khadem (column 7 lines 18-30) does not provide an enabling disclosure.

The Applicant’s submissions have included at least the following:

- The expert opinion of Dr. Michael Hamblin indicating that one of ordinary skill in the art could not have combined Khadem with his [or her] own knowledge to make the claimed invention.
- The Declaration of Dr. Khadem, exemplifying his own failure to create a photochemical bond between tissues without using at least 1% exogenous cross-linkable substrate.
- Lambert et al., (1999) J. Phys. Chem. B, Vol. 103 No. 18, which shows that Rose Bengal is not active within the 600-670 nm wavelength range

taught by Khadem in Table 1, as it does not absorb light within this spectrum.

In response to Applicants' submissions, the Examiner has not provided any explanation that would counter the assertion that one of ordinary skill in the art could not have combined Khadem with his [or her] own knowledge to make the claimed invention. A response reasoned under the proper legal standard is respectfully requested.

**C. Response to Examiner's Comments of September 7, 2005**

The present Office Action, dated September 7, 2005, provides responses to the Applicants' submissions, which will each be addressed in turn.

In referencing M.P.E.P. 716.07, it appears that the Examiner has deemed the Declarations of Dr. Michael Hamblin to be "immaterial" because the claims allegedly do not distinguish the claimed invention from the inoperative reference disclosure. The claims are directed to photochemical methods of tissue bonding or corneal repair in the absence of an exogenous cross-linkable substrate. Khadem does not disclose a method of forming a tissue seal having tensile strength in the absence of an exogenous cross-linkable substrate. The amended claims distinguish over Khadem in that they require the formation of a tissue seal having tensile strength in the absence of an exogenous cross-linkable substrate. Because the claims distinguish the claimed invention from Khadem, the Declarations of Dr. Michael Hamblin are not immaterial under M.P.E.P. 716.07.

The next point alleges that "the 'effect' or the seal are not positively recited" in the claimed method for creating a tissue seal. The last line of claim 1 positively recites the tissue seal and by entry of the amendment, qualifies the effectiveness of the seal as having tensile strength. Likewise, by entry of the amendment, claims 12 and 17 qualify the effectiveness of the corneal seal according to the intraocular pressure limit of the repaired corneal lesion.

Finally, it is alleged that the Declaration of Dr. Khadem was submitted to show that he did not intend to disclose the claimed invention and is therefore, immaterial. M.P.E.P. 716.07, which the Examiner is apparently relying on to discount the Khadem Declaration, was designed to prevent an applicant from soliciting an inventor of a patent cited against applicant's claims to make a declaration that the substance of applicant's claims was not what the inventor had intended to cover in his/her patent. In other words,

M.P.E.P. 716.07 was designed to prevent collusion between a patent applicant and an earlier patentee.

That is certainly not the case here. Dr. Khadem was not solicited by Applicants in the instant application to make the Khadem Declaration, nor are Applicants submitting the Declaration of Dr. Khadem to show that he had no intent to disclose the claimed invention.

In fact, Applicants obtained the Khadeem Declaration from the prosecution history of the Khadem patent. Dr. Khadeem had submitted the declaration during prosecution of his own patent to support his arguments for patentability. Moreover, Applicants have submitted the Declaration of Dr. Khadem to show that the Khadem patent does not enable the alleged disclosure of Applicants' claimed invention because, as set forth in the Khadem Declaration, Dr. Khadem himself stated that he could not perform the claimed invention. Thus, the Declaration of Dr. Khadem is not immaterial under M.P.E.P. 716.07.

In view of all evidence of record, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) is respectfully requested.

**IV. The Rejections Under 35 U.S.C. § 103(a) Are Overcome****A. Rejection of Claims 15-17 and 32-34.**

Claims 15-16 and 24-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Khadem. Claims 15-16 and 24-25 relate to ranges of time, energy doses and irradiances to be used in delivering light. These ranges are alleged to be the result of routine optimization by the skilled artisan and therefore obvious given the teaching by Khadem. *See* pages 5-6 of the Office Action. Applicants respectfully traverse the rejection.

The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir. 1991). Thus, evidence showing that there was no reasonable expectation of success can support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048 (C.C.P.A. 1976).

Claims 15-16 and 24-25 encompass methods of photochemical tissue bonding or corneal repair that exclude the use of an exogenous cross-linkable substrate. Claim 24 depends from claim 1. Claim 1, which relates to photochemical tissue bonding, has been amended to further characterize the tissue seal as having the tensile strength of the native tissue. Claims 15, 16 and 25 depend from claim 12. Claim 12, which relates to corneal repair, has been amended to specify that the intraocular pressure limit of the repaired corneal lesion is greater than 100 mm Hg.

As the teachings of the Khadem Declaration show, there was no reasonable expectation of success in practicing the claimed methods. The Declaration of Dr. Khadem characterizes the strength of the “adhesive connection” allegedly described by Khadem (column 7 lines 18-30), wherein the photosensitizer composition applied to the tissue to form the connection contains less than 1% exogenous protein (i.e., this would include compositions having no exogenous protein). It was demonstrated by Dr. Khadem that use of less than 1% exogenous protein provides no adhesive connection in corneal tissue (bursting pressure was 0.0 mm Hg). *See* paragraph 9 of the Khadem declaration. Consequently, Khadem provides no reasonable expectation of success in practicing the claimed methods.

If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Claims 15-16 and 25 depend from claim 12 and claim 24 depends from claim 1. As the disclosure in Khadem and the knowledge in the art provides no reasonable expectation of success in practicing claims 1 and 12, thereby establishing the nonobviousness of claims 1 and 12, claims 15-16 and 24-25 are by extension also nonobviousness.

Reconsideration and withdrawal of the rejections of claims 15-16 and 24-25 under 35 U.S.C. § 103 is respectfully requested.



**REQUEST FOR AN INTERVIEW**

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

**CONCLUSION**

In view of the amendments and remarks herewith, the application is in condition for allowance. Favorable reconsideration of the application, reconsideration, and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

Respectfully submitted,



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# McGraw-Hill Dictionary of **PHYSICS**

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**TEM wave** See transverse electromagnetic wave.

**Ton Broecke chart** [THERMO] A graphical plot of heat transfer and temperature differences used to calculate the thermal efficiency of a countercurrent cool-fluid-warm-fluid heat-exchange system.

**tenebrescence** [PHYS] Darkening and bleaching under suitable irradiation; materials having this property are called scotophors; darkening may be produced by primary x-rays or cathode rays, while bleaching may be produced by heat or by photons of appropriate wavelength.

**tensile modulus** [MECH] The tangent or secant modulus of elasticity of a material in tension.

**tensile strength** [MECH] The maximum stress a material subjected to a stretching load can withstand without tearing. Also known as hot strength.

**tensile stress** [MECH] Stress developed by a material bearing a tensile load.

**tension** [MECH] 1. The condition of a string, wire, or rod that is stretched between two points. 2. The force exerted by the stretched object on a support.

**tensor force** [NUC PHYS] A spin-dependent force between nucleons, having the same form as the interaction between magnetic dipoles; it is introduced to account for the observed values of the magnetic dipole moment and electric quadrupole moment of the deuteron.

**terahertz** [PHYS] A unit of frequency, equal to  $10^{12}$  hertz, or 1,000,000 megahertz. Abbreviated THz.

**teraohm** [ELEC] A unit of electrical resistance, equal to  $10^{12}$  ohms, or 1,000,000 megohms. Abbreviated TΩ.

**terawatt** [PHYS] A unit of power, equal to  $10^{12}$  watts, or 1,000,000 megawatts. Abbreviated TW.

**tercentesimal thermometric scale** See approximate absolute temperature.

**term** [SPECT] A set of  $(2S + 1)(2L + 1)$  atomic states belonging to a definite configuration and to definite spin and orbital angular momentum quantum numbers  $S$  and  $L$ .

**terminal** [ELEC] 1. A screw, soldering lug, or other point to which electric connections can be made. Also known as electric terminal. 2. The equipment at the end of a microwave relay system or other communication channel. 3. One of the electric input or output points of a circuit or component.

**terminal board** [ELEC] An insulating mounting for terminal connections. Also known as terminal strip.

**terminal box** [ELEC] An enclosure which includes, mounts, and protects one or more terminals or terminal boards; it may include a cover and such accessories as mounting hardware, brackets, locks, and conduit fittings.

**terminal cutout pairs** [ELEC] Numbered, designated pairs brought out of a cable at a terminal.

**terminal leg** See terminal stub.

**terminal pair** [ELEC] An associated pair of accessible terminals, such as the input or output terminals of a device or network.

**terminal strip** See terminal board.

**terminal stub** [ELEC] Piece of cable that comes with a cable terminal for splicing into the main cable. Also known as terminal leg.

**terminal velocity** [FL MECH] The velocity with which a body moves relative to a fluid when the resultant force acting on it (due to friction, gravity, and so forth) is zero. [PHYS] The maximum velocity attainable, especially by a freely falling body, under given conditions.

**terminal voltage** [ELEC] The voltage at the terminals connected to the source of electricity for an electric machine.

terminated line  
characteristic impedance

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